## REMARKS

Upon entry of the amendment, claims 13, 16-21, 24-28, and 31-52 will be pending in the application. Support for new claims 51 and 52 appears in the specification at, e.g, page 22, lines 1-4. No new matter is added.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 13, 16-21, 24-28, and 31-50 are rejected for lack of enablement. The Office states that antibody-based therapies are generally unpredictable and concludes that the specification is not enabling for the treatment and prevention of tissue fibrosis using antibodies that bind IL-13. Relying on Choy (Cytokine 28: 158-161, 2004; "Choy") and Borrebaeck et al. (Current Opinion in Pharmacology, 1: 404-408, 2001; "Borrebaeck") for example, the Office, while acknowledging the successful use of antibody-based therapies, points to side-effects that may be associated with the administration of antibodies, such as an anti-TNF antibody. Based on such teachings, the Examiner concludes that in vivo studies must be performed to properly evaluate the efficacy and safety of antibodies. For the reasons outlined below, each of these bases for the rejection are respectfully traversed.

First, regarding the Office's assertion that *in vivo* experimental data must be presented in the specification, Applicants note that the case law does not support such a requirement. In fact, the M.P.E.P. clearly states (emphasis added):

> *An applicant need not have actually reduced the invention to practice prior to filing.* In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987), as of Gould's filing date, no person had built a light amplifier or measured a population inversion in a gas discharge. The Court held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA) 1956)).

Furthermore, the case law is clear that "[t]he specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without undue experimentation. *In re Borkowski,* 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)." Thus, the lack of any examples, let alone *in vivo* working examples, does not compel a conclusion that the present specification not enabled. Because Applicants' specification provides extensive enabling details concerning the administration of an antibody or fragment of an antibody that binds IL-13 for the purpose of treating or preventing tissue fibrosis, one skilled in the art would know how to carry out the claimed invention. On this basis alone, the rejection should be withdrawn.

The Office's reliance on the general state of antibody-based therapies is also an inappropriate basis for concluding that Applicants' methods are not enabled. To emphasize the unpredictability of antibody-based therapy strategies, the Examiner cites Choy, a review that describes various TNF antagonists and side-effects that may be associated with their use. There is no suggestion in the reference however that these side effects are caused by or even related to the use of antibodies. Rather, the reference implies that the increased rates of infections is caused by modulating the activity of TNF in the patient. The Examiner further cites Borrebaeck that, if anything emphasizes that the use of antibodies in the clinic is not unpredictable. Although the Examiner contends that "there is a chance that the mammal might develop a response against these antibodies," Borrebaeck explicitly states that problems of such nature were encountered in the early 1980s and have been resolved with improved protein engineering techniques (see page 404, column 1 and column 2). To highlight the efficacy of therapeutic antibodies, Borrebaeck goes on to mention that antibodies makes up 30% of all clinical trials and even states that "[t]he above examples of antibody-based in cancer, considered to be one of the

most difficult indications, clearly show that antibodies can exert a quite impressive clinical effect compared with that shown in earlier trials, at least within leukaemia/lymphoma malignancy." (See paragraph bridging column 1 and 2, page 405). Moreover, the claims require a therapeutically effective amount of antibody and, to the extent an antibody elicits side effects that negate it effectiveness, specifically exclude the antibody.

In view of the above, Applicants respectfully disagree with the Examiner's position on the lack of success of antibody-based strategies and submit that the use of therapeutic antibodies is in fact predictable. As evidence of this assertion, Applicant point the Examiner's attention to a study by Yang et al. (Cytokine 28: 224-232, 2004; "Yang"; submitted as Exhibit A), where the use of a monoclonal antibody to IL-13 in a chronic asthma model successfully reduced the level of subepithelial fibrosis, an airway structural change that negatively impacts airway functions (see page 225, first column, line 15 of second paragraph and page 227, first column, second paragraph to page 228, first column, first paragraph). In view of this study, Applicants submit that there can be no question that a person of ordinary skill in the art could have practiced the present invention without undue experimentation using the teachings in the specification and standard molecular biology techniques. Moreover, given the success achieved with other therapeutic antibodies, Applicants submit that there is a high level of predictability for a positive therapeutic outcome. The § 112, first paragraph rejection should be withdrawn.

A petition for extension of time accompanies this response. The Commissioner is authorized to charge any additional fees that may be due, or to credit any overpayment, to the undersigned's account, Deposit Account No. 50-0311 Ref. No. 22058-519 CIPDIV2.

Respectfully submitted,

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